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# Calciophylaxis

The enigma

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**6<sup>th</sup>** International Annual MNDU conference (NEPHRO-MANSOURA)  
2016

**Mona Tawfik**

Lecturer of internal Medicine  
Nephrology Unit  
MNDU

# Calciophylaxis

**A disorder of  
calcification and thrombosis of dermal  
arterioles leading to painful skin  
lesions**

Case report

**Open Access**

## **A 44 year-old lady with chronic renal disease and intractable ulcers: a case report**

Thejeswi Pujar\*<sup>1,3</sup> and Irene M Spinello<sup>2,3</sup>

Published: 31 July 2009



# Calciophylaxis

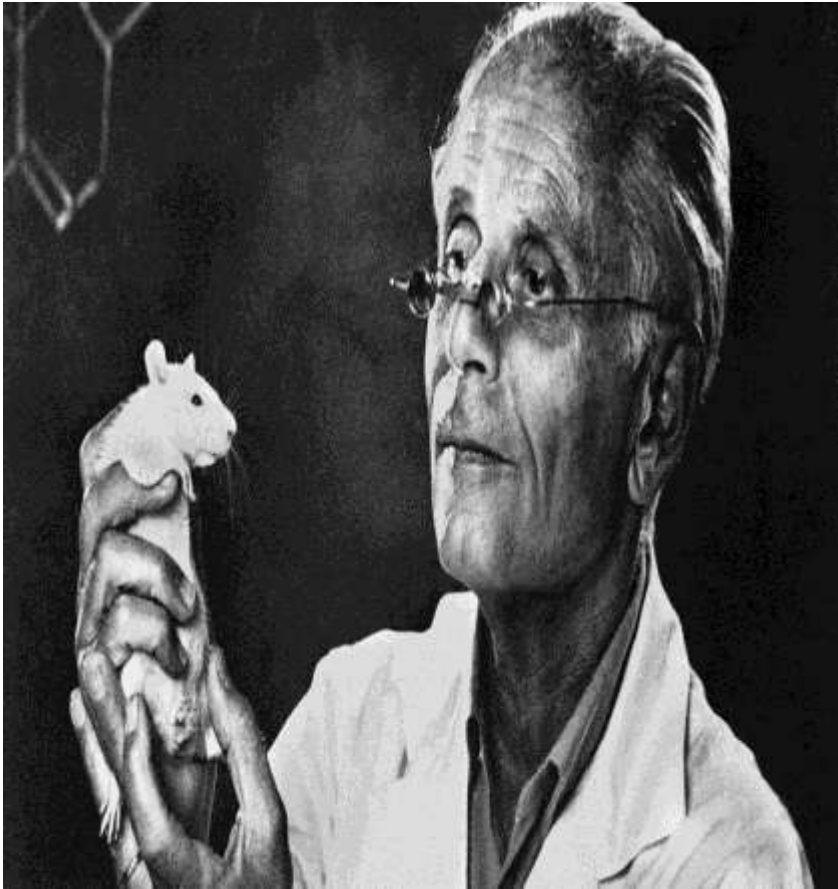
- ☐ HD patient
- ☐ Early CKD patient
- ☐ Patients with normal kidney function

# AGENDA

- ❑ Historical perspectives
- ❑ Epidemiology and magnitude of the problem
- ❑ Risk factors for calciphylaxis
- ❑ Diagnosis and evaluation
- ❑ Mimics of calciphylaxis
- ❑ Treatment strategies

# Historical perspectives & Terminology

# Historical Background



**Hans Selye**

(1907-1982)

The first who  
coined the term  
calciphylaxis in  
1961

# Professor Selye described calciphylaxis as a two-step “phylactic” response



Sensitizing Agents e.g. uremia, parathyroid hormone extract, high phosphorous diet, or vitamin D

“critical period”

Challenging Agents, e.g. trauma, egg albumin, metallic salts



Development of cutaneous calcification in this animal model was thought to be an adaptive or phylactic reaction and was referred to as

**calciphylaxis**

(portmanteau of **calcification** and **phylaxis**).



*Selye et al. Science. 1961*



# Early reports of human calciphylaxis



Fig. 2—Right thigh on July 1, 1966, before sloughing of necrotic fat.

Anderson , et al , Lancet , 1968

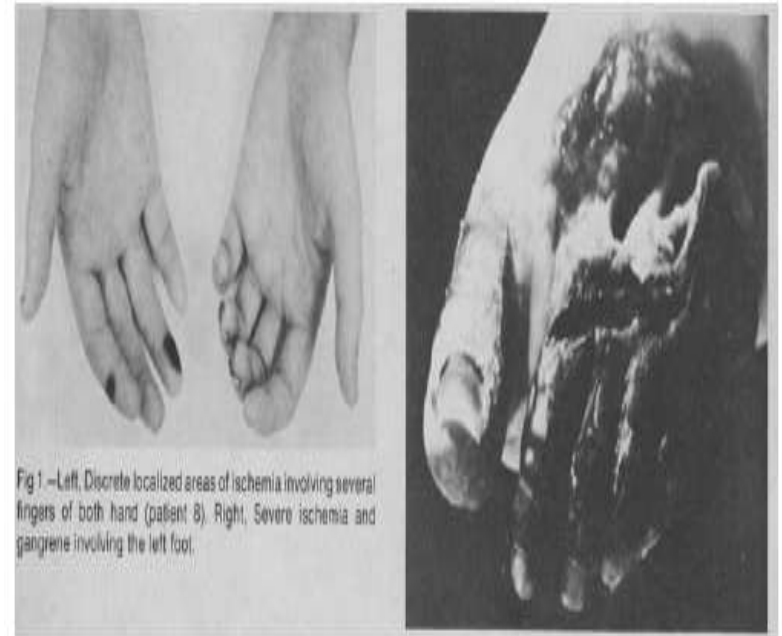


Fig 1—Left, Discrete localized areas of ischemia involving several fingers of both hand (patient 8). Right, Severe ischemia and gangrene involving the left foot.

Gipstein , et al, Archive of int med, 1976

# Calciophylaxis VS CUA

## A matter of terminology



1

2

3



*Nigwekar , et al, Am J Kidney Dis. 2015 July ; 66(1): 133–146*

# Calciophylaxis

- ❑ HD patient

( Uremic calcific arteriopathy )

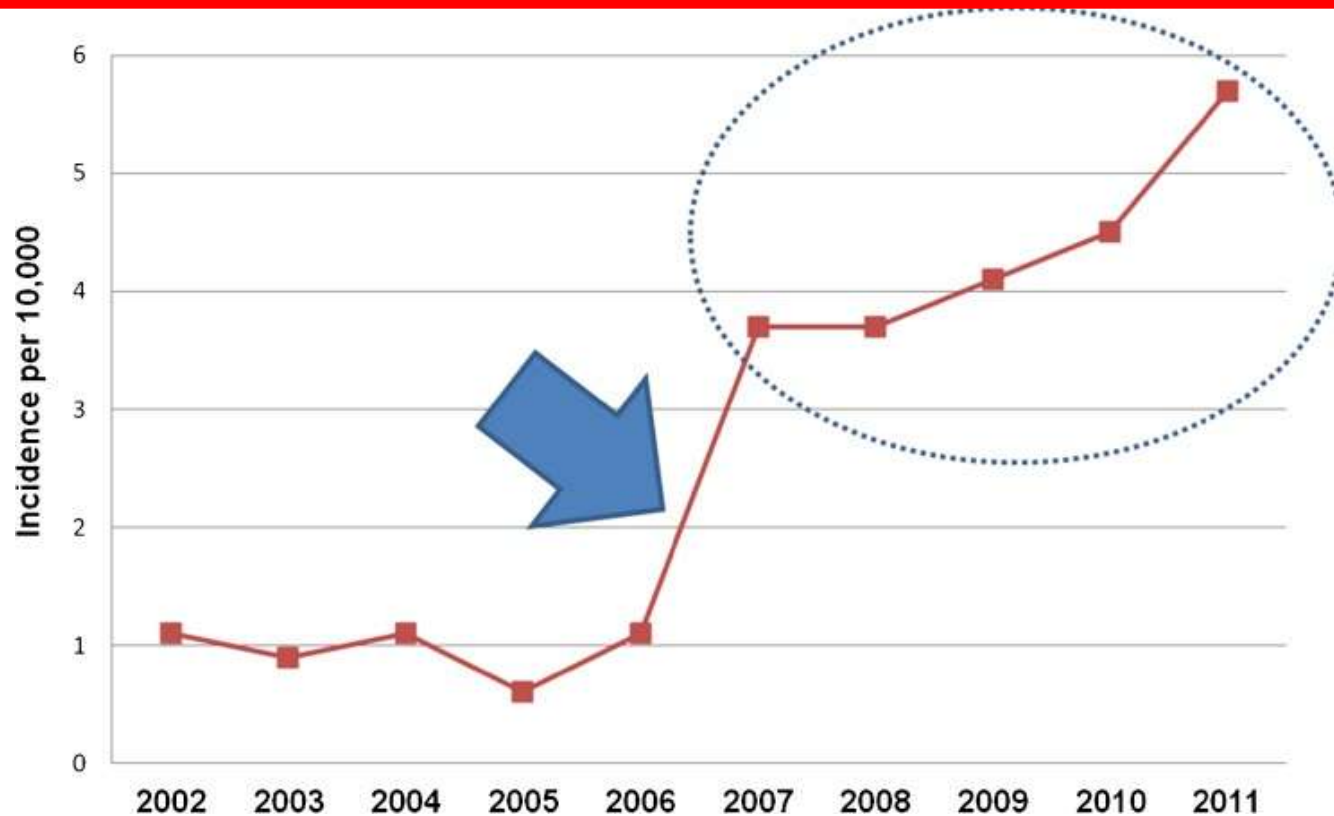
- ❑ Early CKD patient

- ❑ Patients with normal kidney function

( non uremic calcific arteriopathy )

# **Epidemiology & Risk Factors**

# Annual incidence of calciphylaxis in the USRDS



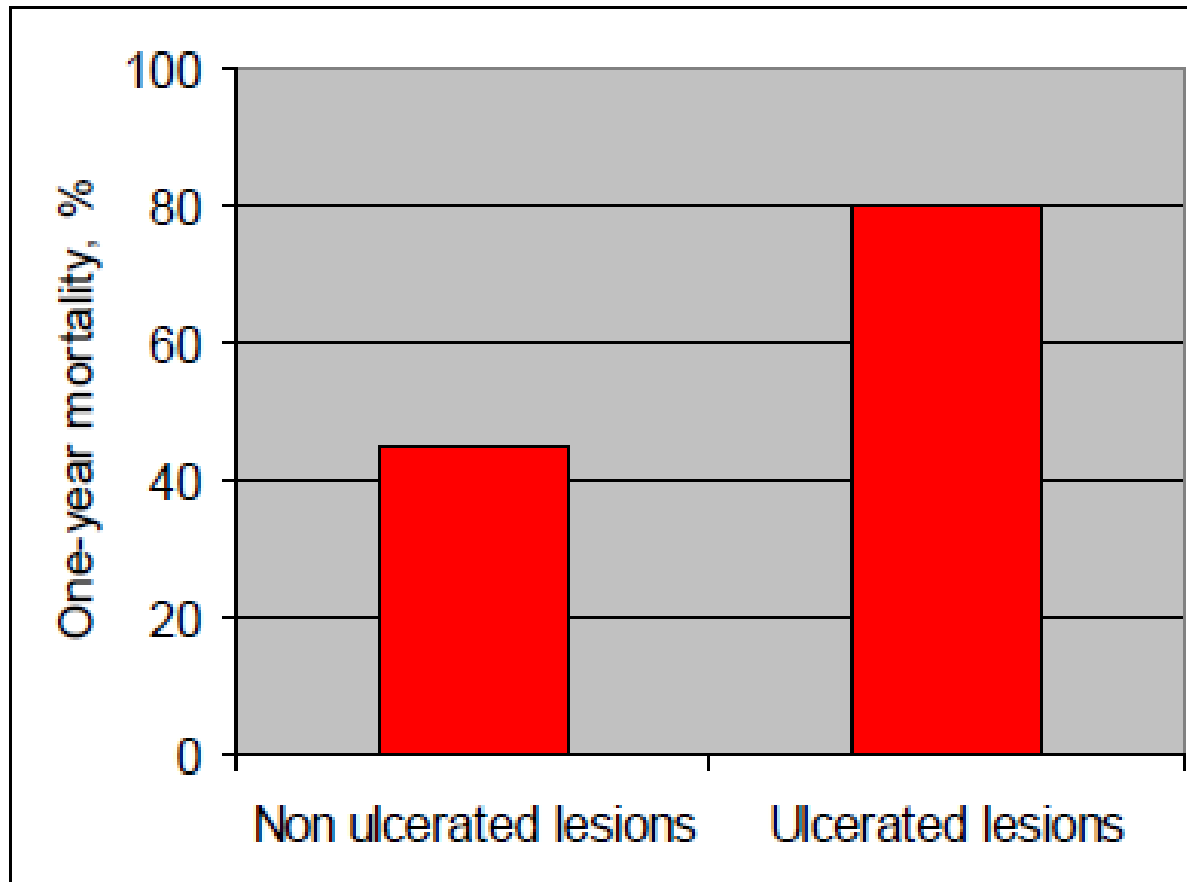
*Nigwekar, et al, J Gen Intern Med, 2014, 29(Suppl 3):S724–31*

*Original Article*

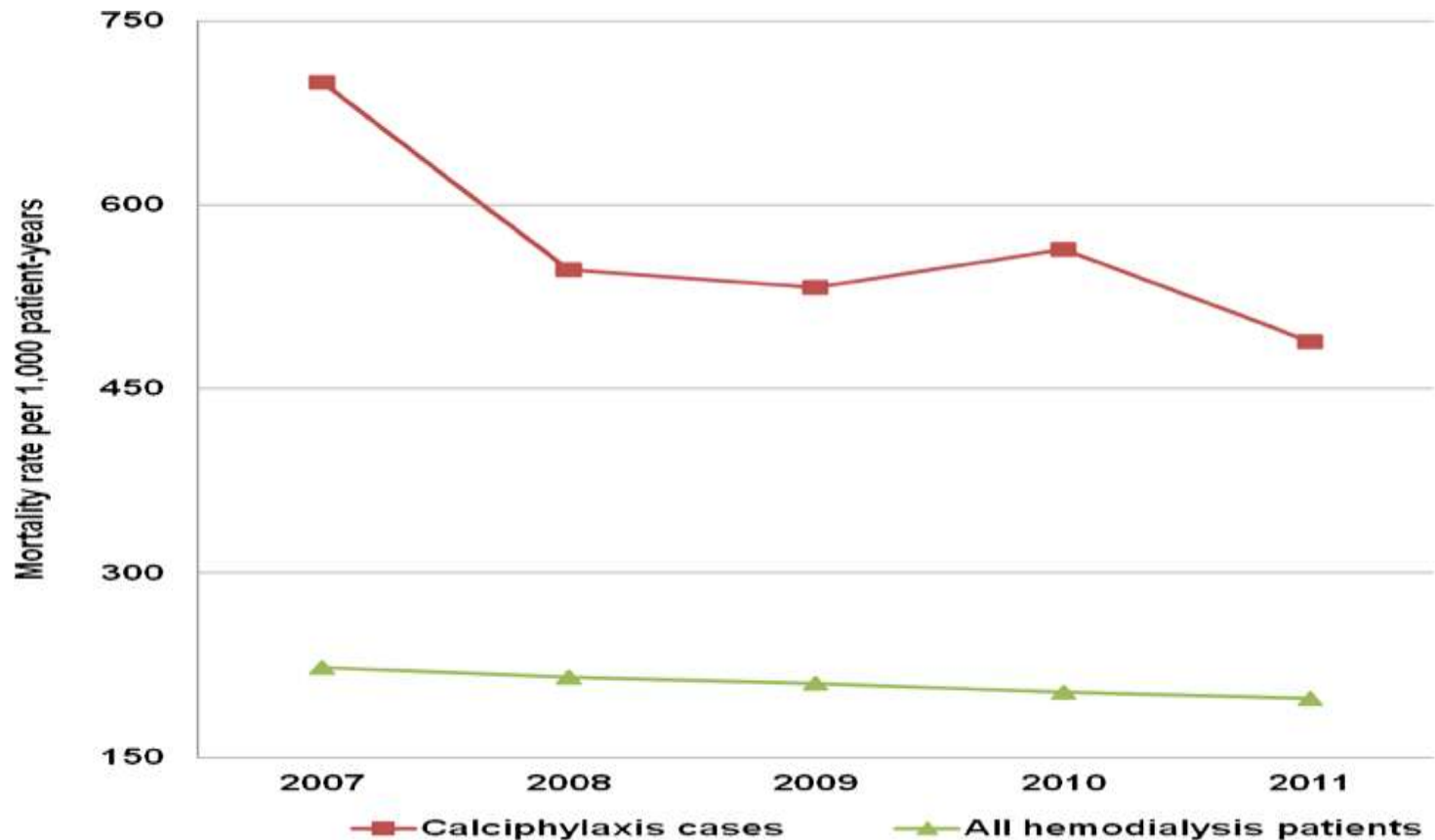
Calcific uraemic arteriolopathy (calciphylaxis): data from a large nationwide registry

Status of kidney disease prior to CUA development ( $n = 253$ )	$n$ (%)
Normal or mildly impaired renal function	7 (3)
CKD, non-dialysis	18 (7)
Functioning kidney graft	10 (4)
PD	25 (10)
Dialysis (HD + HDF)	193 (76)
ESRD (dialysis + transplantation)	228 (90)

# One year mortality in calciphylaxis patients



# Mortality rate per 1,000 patient-years in the USRDS



*Nigwekar, et al, J Gen Intern Med, 2014, 29(Suppl 3):S724–31*



# Problem magnitude

- Both uremic and non-uremic calciphylaxis are associated with significant morbidity and mortality. The morbidity is related to
  1. Severe pain.
  2. Non-healing wounds.
  3. Recurrent hospitalizations
  4. Adverse effects of treatments

## IMAGES IN CLINICAL MEDICINE

## Metastatic Calcification and Long-Term Hemodialysis

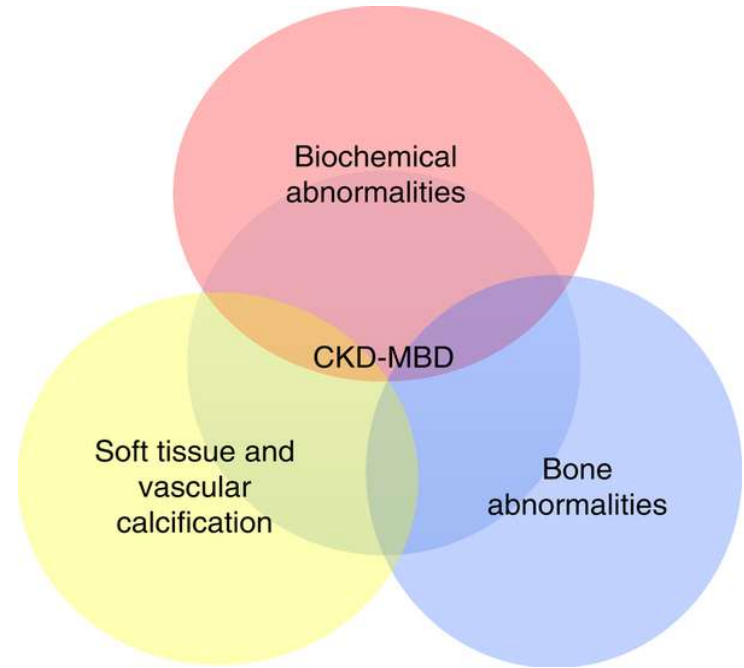
**A**N 80-YEAR-OLD WOMAN PRESENTED WITH LEFT LEG PAIN. SHE HAD END-STAGE RENAL DISEASE CAUSED by hypertensive nephrosclerosis and was undergoing maintenance hemodialysis. A radiograph of the pelvis and femur revealed extensive calcifications (arrow) in the muscles and subcutaneous tissues of the lower abdominal wall, gluteal regions, and outer thighs, in addition to vascular calcification (arrowhead) and osteopenia.



# Risk Factors

## CKD-MBD

- Hyperphosphatemia
- Hypercalcemia
- Elevated Ca , Po<sub>4</sub> product
- Hyperparathyroidism.



Some patients who develop calciphylaxis have neither hypercalcemia nor hyperphosphatemia.

**(*Budisavljevic , 1996 and Bleyer, 1998*)**

## ORIGINAL INVESTIGATIONS

### A Case Control Study of Proximal Calciphylaxis

Anthony J. Bleier, MD, MS, Michael Choi, MD, Benjamin Igwemezie, MD,  
Ernesto de la Torre, BS, and Wain L. White, MD

**The dysregulated calcium-phosphate metabolism alone can not explain the pathogenesis of Calciphylaxis**

# Other Risk Factors

- **Demographics and co-morbidities**

- Caucasian race
- Female gender
- Obesity
- Autoimmune disease
- Hypercoagulable state
- DM

- **Hypoalbuminemia**

- **Medications**

- Calcium-based binders
- Vitamin D
- Warfarin
- Iron therapy
- Corticosteroid therapy

# ORIGINAL INVESTIGATIONS

## A Case Control Study of Proximal Calciphylaxis

Anthony J. Bleyer, MD, MS, Michael Choi, MD, Benjamin Igwemezie, MD,  
Ernesto de la Torre, BS, and Wain L. White, MD

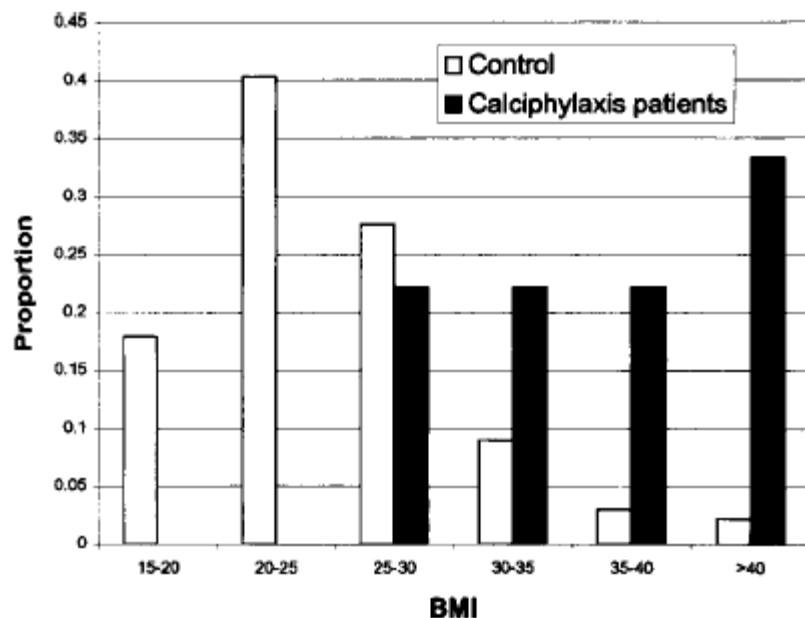


Fig 1. Proportion of calciphylaxis and control patients according to body mass index (BMI).

Table 4. Best-Fit Logistic Regression Model for Factors Associated With Calciphylaxis

Parameter	Reference	Odds Estimate (95% Confidence Interval)
Body mass index	Increase of 1 kg/m <sup>2</sup>	6.29 (3.7-10.7)
Serum albumin	Decrease of 10 g/L	16.9 (5.25-54.5)

# Dialysis vintage

- Longer dialysis vintage of over 6-7 years has been reported as a risk factor for calciphylaxis.
- However, this relationship has been inconsistent across studies and there are reports in the literature of patients with significantly shorter dialysis vintage developing calciphylaxis.

# **Diagnosis & Clinical mimics**



# Diagnosis

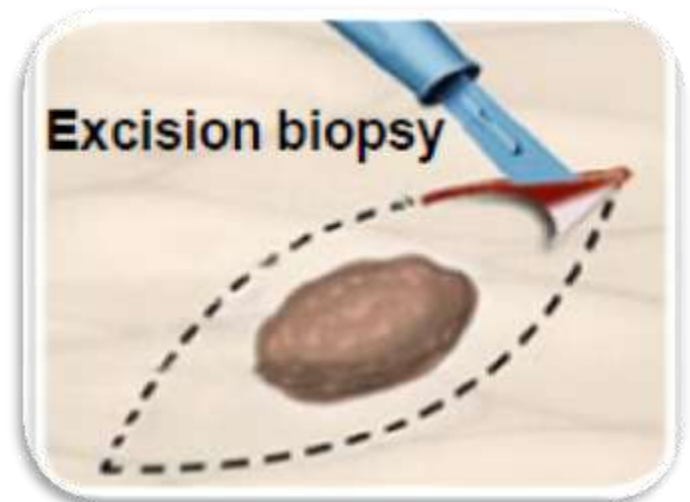
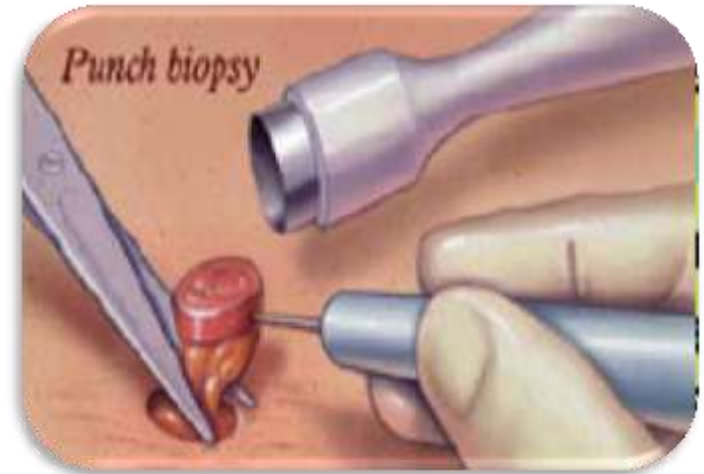
- A high index of clinical suspicion is required for early and accurate diagnosis of calciphylaxis.
- Clinically, it is characterized by very painful plaques or subcutaneous nodules, associated violaceous, mottled skin lesions that may progress to nonhealing ulcers, tissue usually at the fatty areas of abdomen , thigh and buttocks .

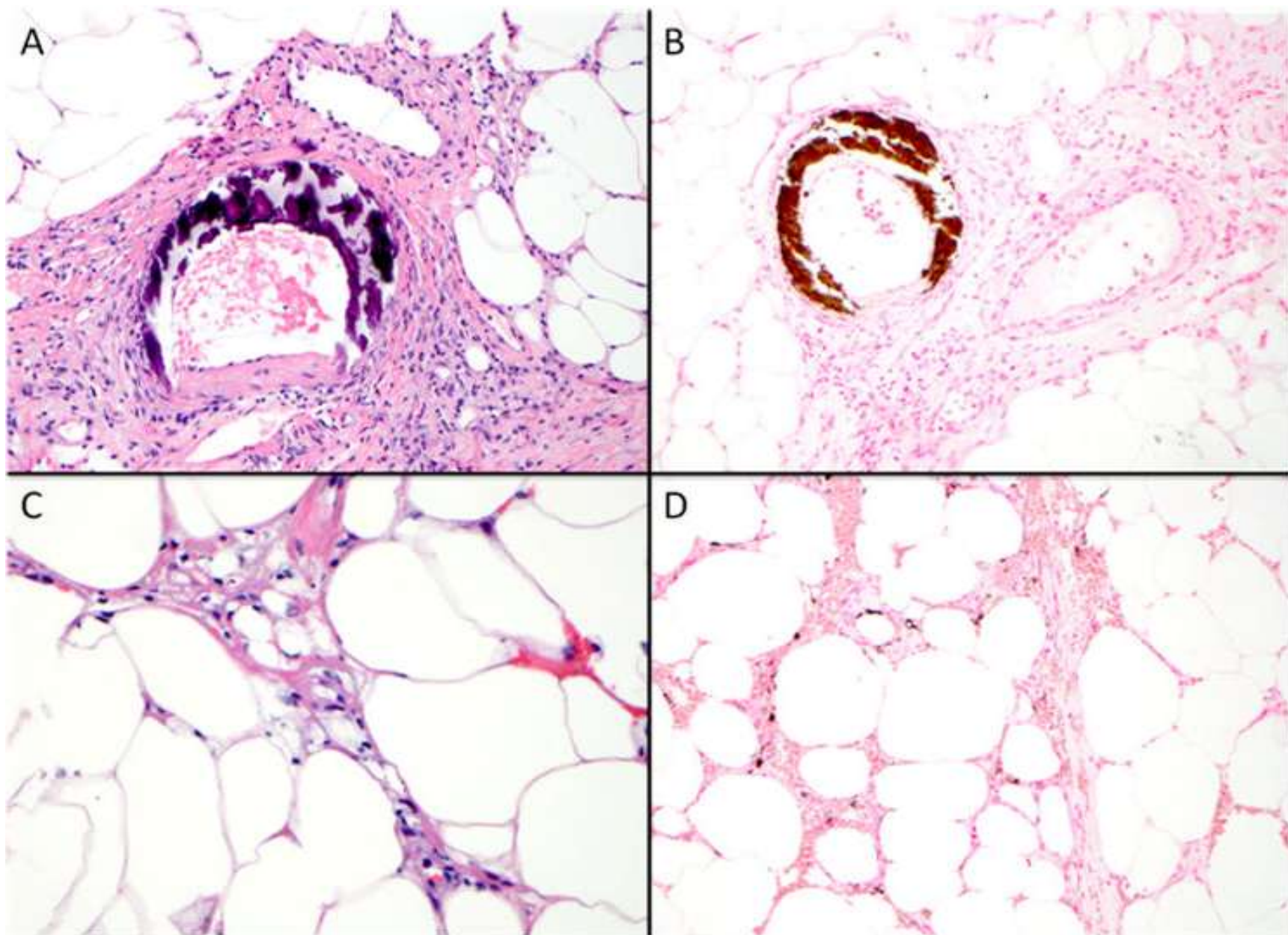
# Gross lesion



# Skin Biopsy

- Possible risks include ulceration, superimposed infection, **propagation of new lesions**, bleeding, and induction of necrosis.
- Benefits include **exclusion** of other conditions that can mimic calciphylaxis

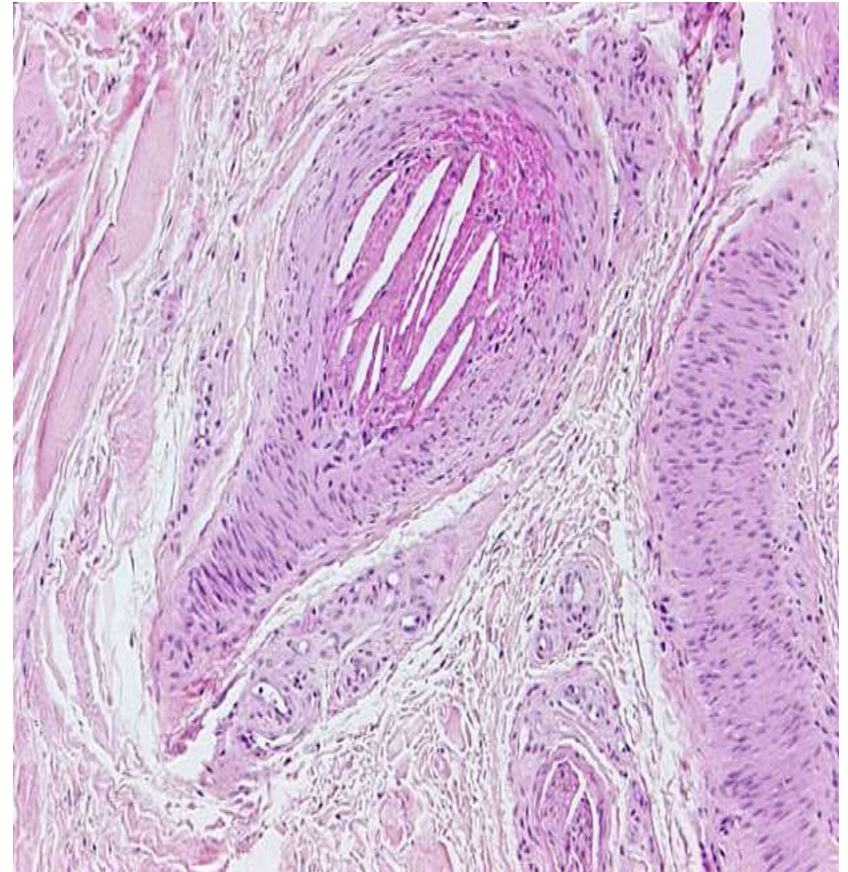






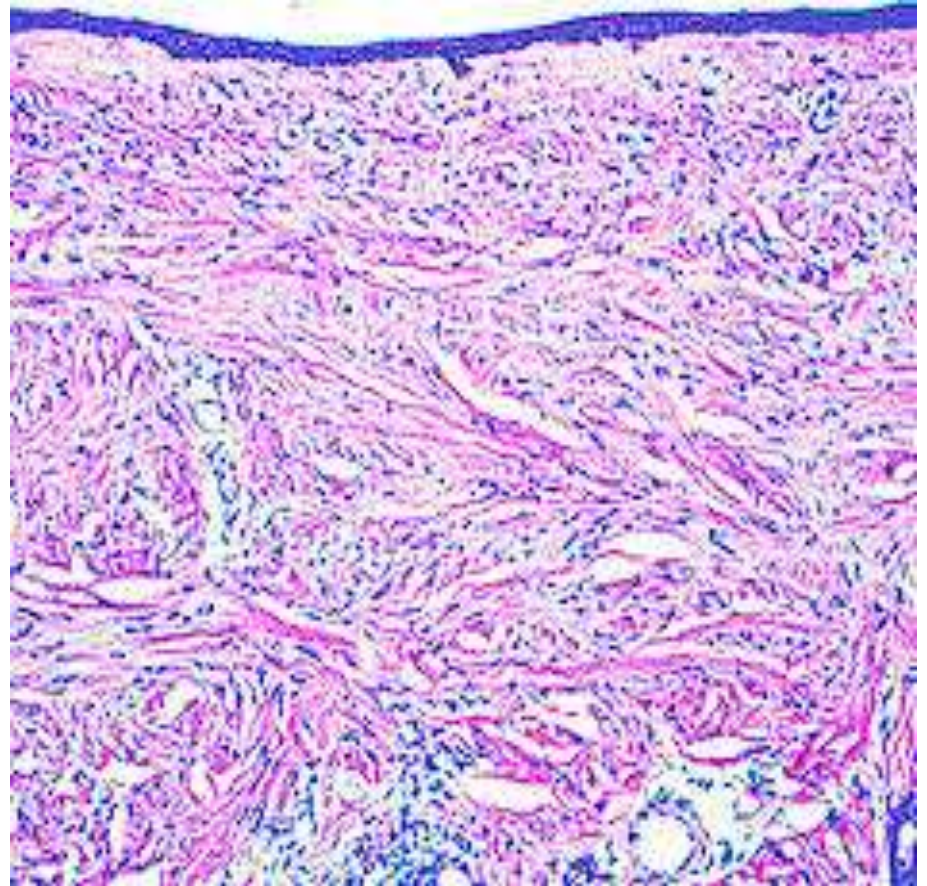
	Features of clinical mimic	Features of calciphylaxis
Atherosclerotic vascular disease	Symptoms of claudication, weak peripheral pulses, distal distribution, abnormal ankle-brachial index	Can be proximal or distal distribution, severe pain, dermal arteriolar calcification on skin biopsy
Cholesterol embolization	Usually in acral distribution, may have features associated with renal or gastrointestinal ischemia, cholesterol clefts on skin biopsy	Can be proximal or distal distribution, dermal arteriolar calcification on skin biopsy
Nephrogenic systemic fibrosis	Brawny plaques, thickened skin, history of exposure to gadolinium, moderate intensity pain, marked increase in spindle cells and fibrosis on skin biopsy	Severe pain, dermal arteriolar calcification on skin biopsy
Oxalate vasculopathy	Acral distribution, history of calcium oxalate stones, birefringent, yellowish-brown, polarizable crystalline material deposition in the dermis and arteriolar wall on skin biopsy	Can be proximal or distal distribution, calcium deposits non-polarizable
Purpura fulminans	Usually seen in the settings such as septic shock or disseminated intravascular coagulation, diffuse body distribution, rapid progression, clinical features of shock	Unlikely to have diffuse whole body distribution, absence of serological features of disseminated intravascular coagulation, dermal arteriolar calcification on skin biopsy
Vasculitis	Systemic features of vasculitis, serological test abnormalities (e.g. cryoglobulins), no dermal arteriolar calcification on skin biopsy, unlikely to have full-thickness necrosis or large areas of involvement	Absence of systemic features and serological abnormalities of vasculitis (unless autoimmune disease is a trigger for calciphylaxis), black eschar, dermal arteriolar calcification on skin biopsy
Warfarin necrosis	Typically seen within the first 10 days of warfarin initiation, manifestation of paradoxical hypercoagulable state created by a transient imbalance in the procoagulant and anticoagulant pathways warfarin discontinuation associated with clinical improvement in majority of cases	Warfarin exposure of prolonged duration when calciphylaxis associated with warfarin therapy, black eschar, dermal arteriolar calcification on skin biopsy

# Cholesterol emboli

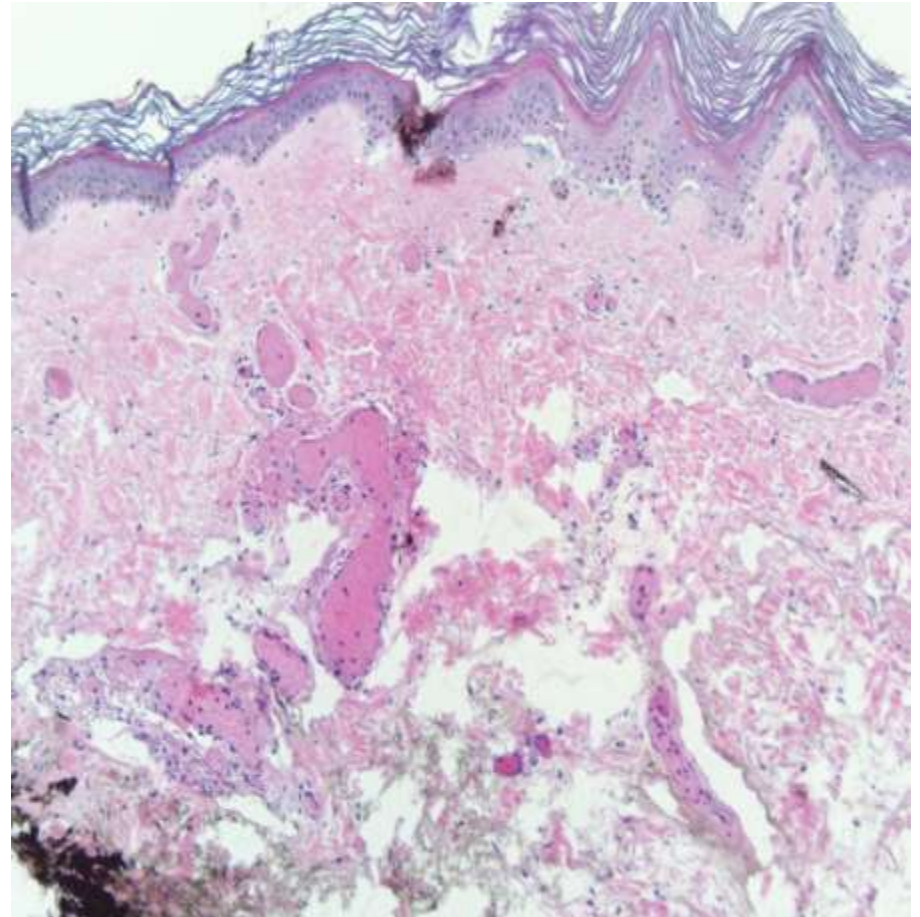




# Nephrogenic systemic fibrosis

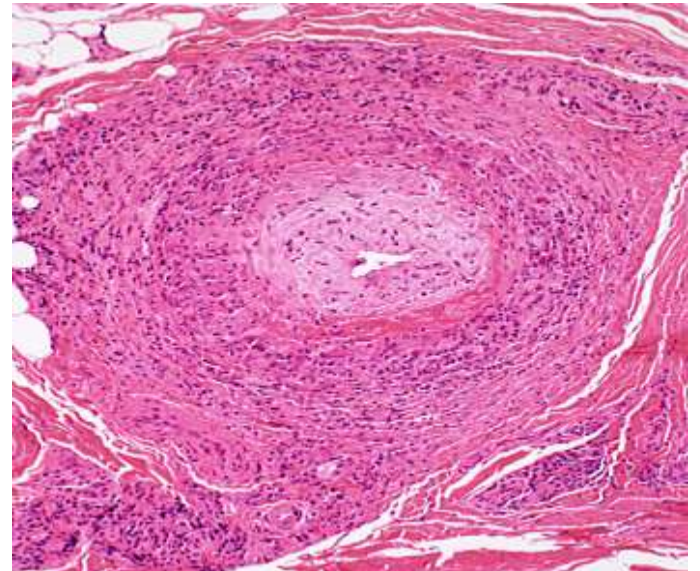
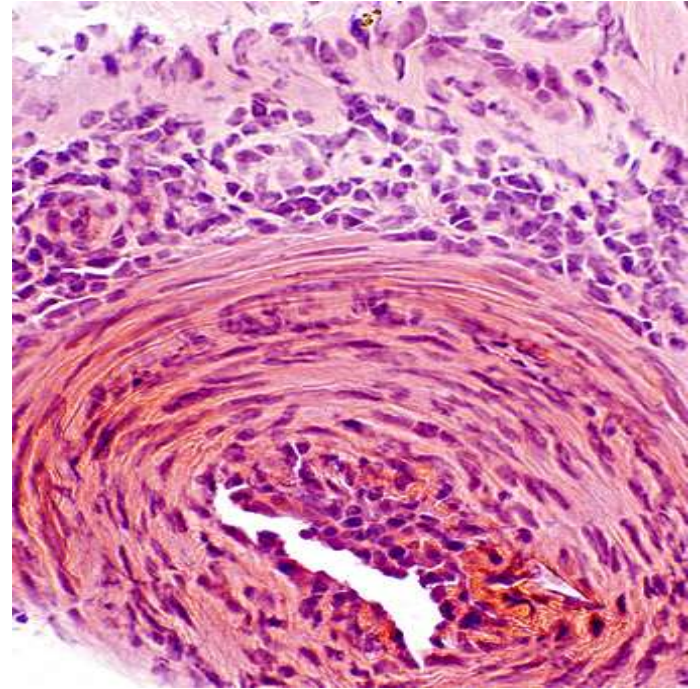


# Warfarin Necrosis





# Vasculitis



# Purpura Fulminans





# Oxalate Vasculopathy



# **Radiological tests and biomarkers**

## **Non-invasive imaging tools**

1. Plain X-rays
2. Nuclear bone scans
3. Circulating fetuin A levels

## Net-like pattern of calcification on plain soft-tissue radiographs in patients with calciphylaxis

Radiographic finding	Sensitivity (%)	Specificity (%)	Odds ratio*	P value
Presence of vascular calcification	89.7	44.8	7.0 (1.9-25.9)	.003
Presence of small-vessel calcification	62.1	81.0	7.0 (2.6-18.9)	<.001
Netlike pattern of calcification	55.2	89.7	10.7 (3.5-32.6)	<.001

### CAPSULE SUMMARY

- Calciphylaxis is a rare, life-threatening syndrome marked by vascular calcification and cutaneous necrosis.
- The role of radiographic imaging in assisting in diagnosis has not been established.
- A netlike pattern of calcification on plain radiographs of any body part, including areas without visible skin lesions, is a notable feature that may assist in the diagnosis of calciphylaxis.



## CASE REPORT

# Calciophylaxis and bone scintigraphy: case report with histological confirmation and review of the literature

**In summary, a bone scan can help diagnose, evaluate the real extent of the disease, and track the response to treatment in patients with calciophylaxis. Thus, a bone scan could also be proposed as a prognostic indicator because systemic involvement appears to be associated with a poor prognosis even in cases that present with localized clinical symptoms .**

# The serum protein $\alpha_2$ -Heremans-Schmid glycoprotein/fetuin-A is a systemically acting inhibitor of ectopic calcification

Cora Schäfer,<sup>1</sup> Alexander Heiss,<sup>1</sup> Anke Schwarz,<sup>2</sup> Ralf Westenfeld,<sup>1,3</sup> Markus Ketteler,<sup>3</sup> Jürgen Floege,<sup>3</sup> Werner Müller-Esterl,<sup>4</sup> Thorsten Schinke,<sup>5</sup> and Willi Jahnke-Dechent<sup>1</sup>

+/+



-/-



**b**

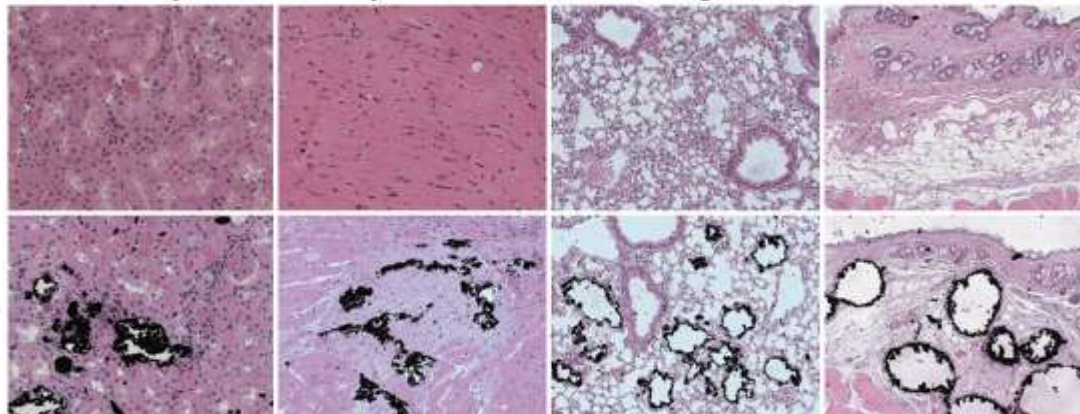
Kidney

Myocard

Lung

Skin

+/+

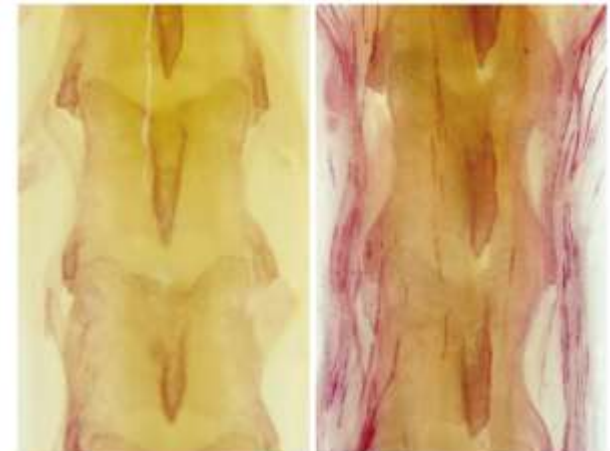


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**a**

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# HHS Public Access

Author manuscript

*Am J Kidney Dis.* Author manuscript; available in PMC 2015 December 30.

Published in final edited form as:

*Am J Kidney Dis.* 2015 July ; 66(1): 133–146. doi:10.1053/j.ajkd.2015.01.034.

## Calciophylaxis: Risk Factors, Diagnosis, and Treatment

Sagar U. Nigwekar, MD, MMSc<sup>±</sup>, Daniela Kroshinsky, MD, MPH<sup>\*</sup>, Rosalynn M. Nazarian, MD<sup>Ω</sup>, Jeremy Gorman, MD<sup>Φ</sup>, Rajeev Malhotra, MD<sup>¶</sup>, Vicki Ann Jackson, MD, MPH<sup>∞</sup>, Mihir M. Kamdar, MD<sup>∞</sup>, David Steele J.R., MD<sup>±</sup>, and Ravi I. Thadhani, MD, MPH<sup>±</sup>

### Radiological tests and biomarkers

Non-invasive imaging tools (e.g. plain X-rays, nuclear bone scans) and circulating fetuin A levels have been reported to aid in the diagnosis of calciophylaxis.<sup>66-69</sup> However, none of these tools have been systematically evaluated and are not recommended for clinical use at this time.



# Laboratory investigations

**Laboratory evaluation should be conducted to further evaluate potential risk factors and exclude mimics of calciphylaxis**

- 1) Renal function evaluation-
- 2) Mineral bone parameters evaluation-
- 3) Liver evaluation-serum transaminases, alkaline phosphatase, and albumin,
- 4) Infection evaluation
- 5) Coagulation evaluation
- 6) Inflammation evaluation
- 7) Hypercoagulation evaluation
- 8) Evaluation for autoimmune disease and malignancy as guided by the clinical suspicion.

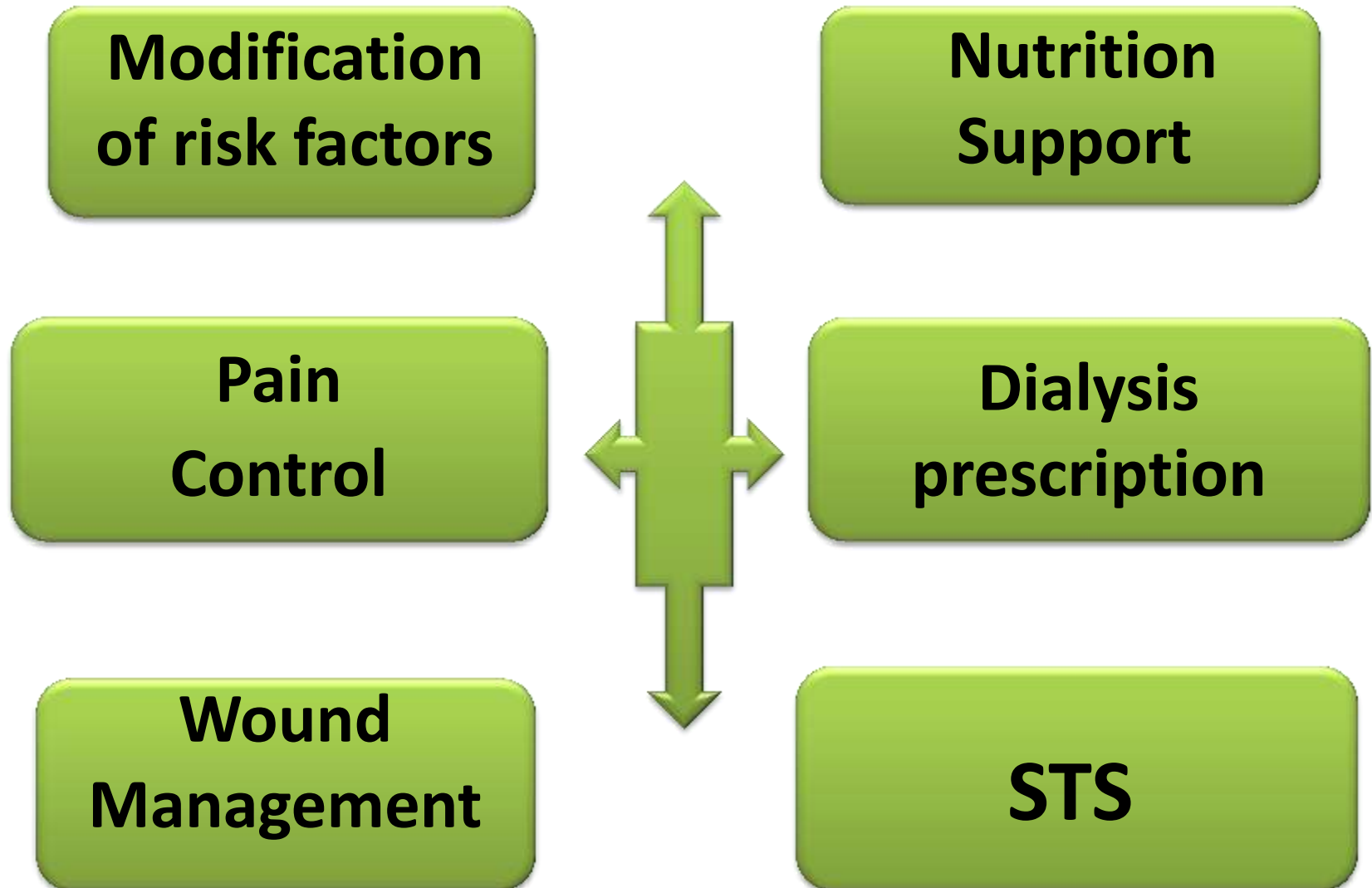
# **Prevention & Treatment**

# Research Gap

The overall **quality of evidence is poor** and data mostly come from retrospective cohort studies, case series, and case reports. There is no published data from a randomized controlled trial that addresses any of the proposed interventions.

An expert opinion based on the clinical experience and available observational published data guide the treatment strategies

# Calciphylaxis Treatment



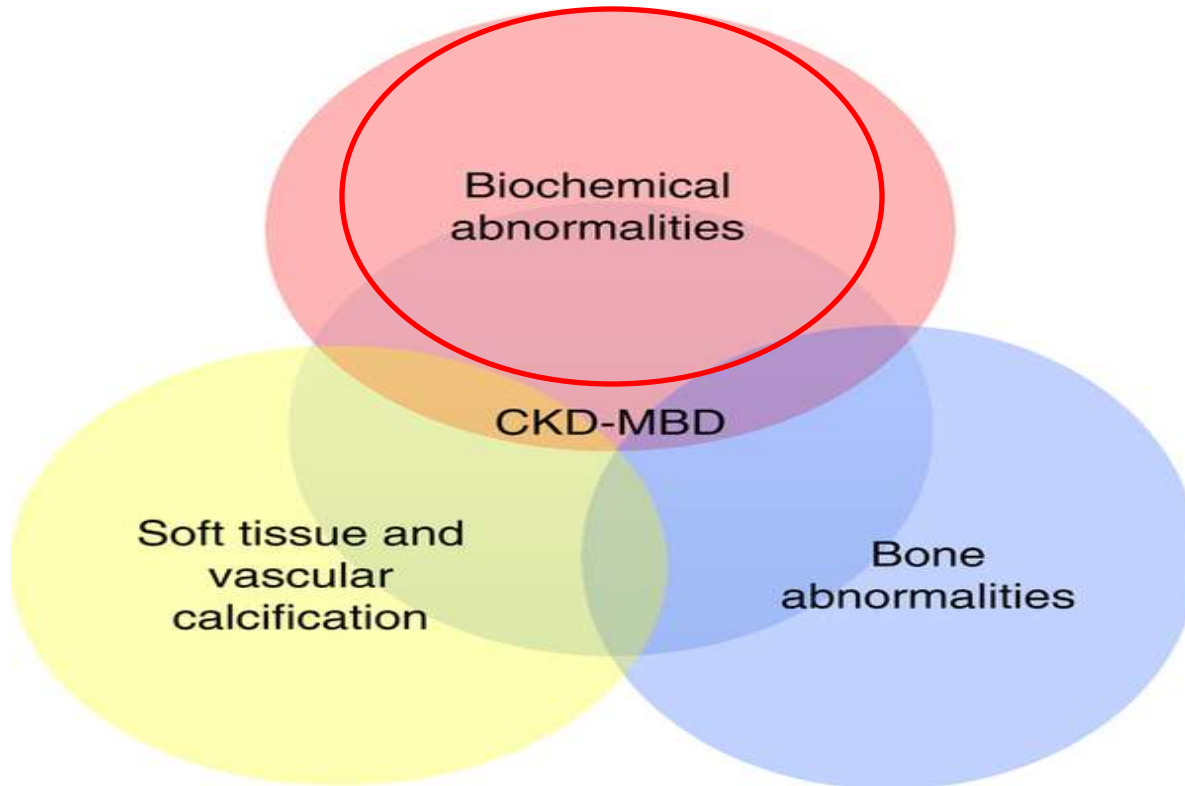
# Treatment

**A multi-disciplinary and multi-interventional approach is important**

- ☐ Nephrology
- ☐ Dermatology
- ☐ Dermatopathology
- ☐ Burn and plastic Surgery
- ☐ Nutrition
- ☐ Pain management



# Prevention and TTT of CKD-MBD



**Caution with vitamin D and calcium supplementation with close monitoring of calcium, phosphorus, and PTH homeostasis is recommended**



# HHS Public Access

Author manuscript

*Am J Kidney Dis.* Author manuscript; available in PMC 2015 December 30.

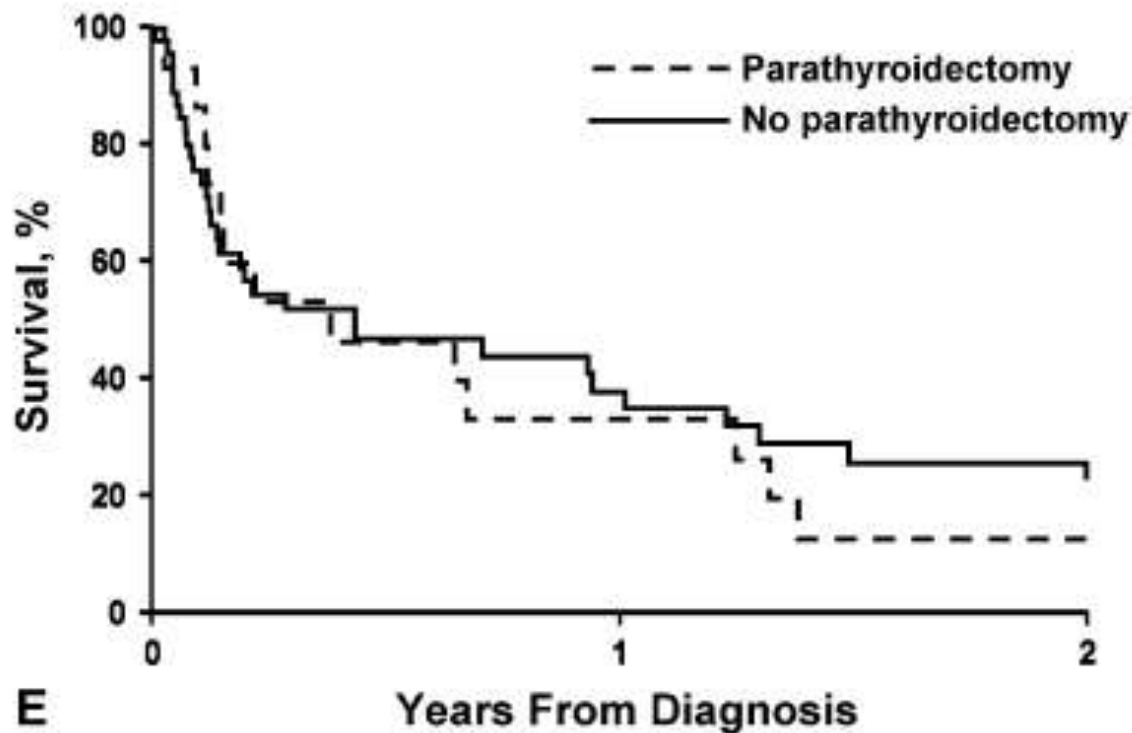
Published in final edited form as:

*Am J Kidney Dis.* 2015 July ; 66(1): 133–146. doi:10.1053/j.ajkd.2015.01.034.

## Management of mineral bone disease

- Serum calcium and phosphorous levels should be maintained in the normal range and serum parathyroid hormone level should be maintained between 150-300 ng/mL.
- Calcium supplements, high dialysate calcium bath, vitamin D preparations should be avoided and instead cinacalcet to be considered to treat secondary hyperparathyroidism in patients with calciphylaxis. Surgical parathyroidectomy is indicated in patients with refractory hyperparathyroidism.
- Excessive suppression of parathyroid hormone should be avoided.<sup>99</sup>

# Patients with calciphylaxis who had parathyroidectomy compared with those who did not





# Risk of parathyroidectomy

The risks of parathyroidectomy in calciphylaxis patients includes:

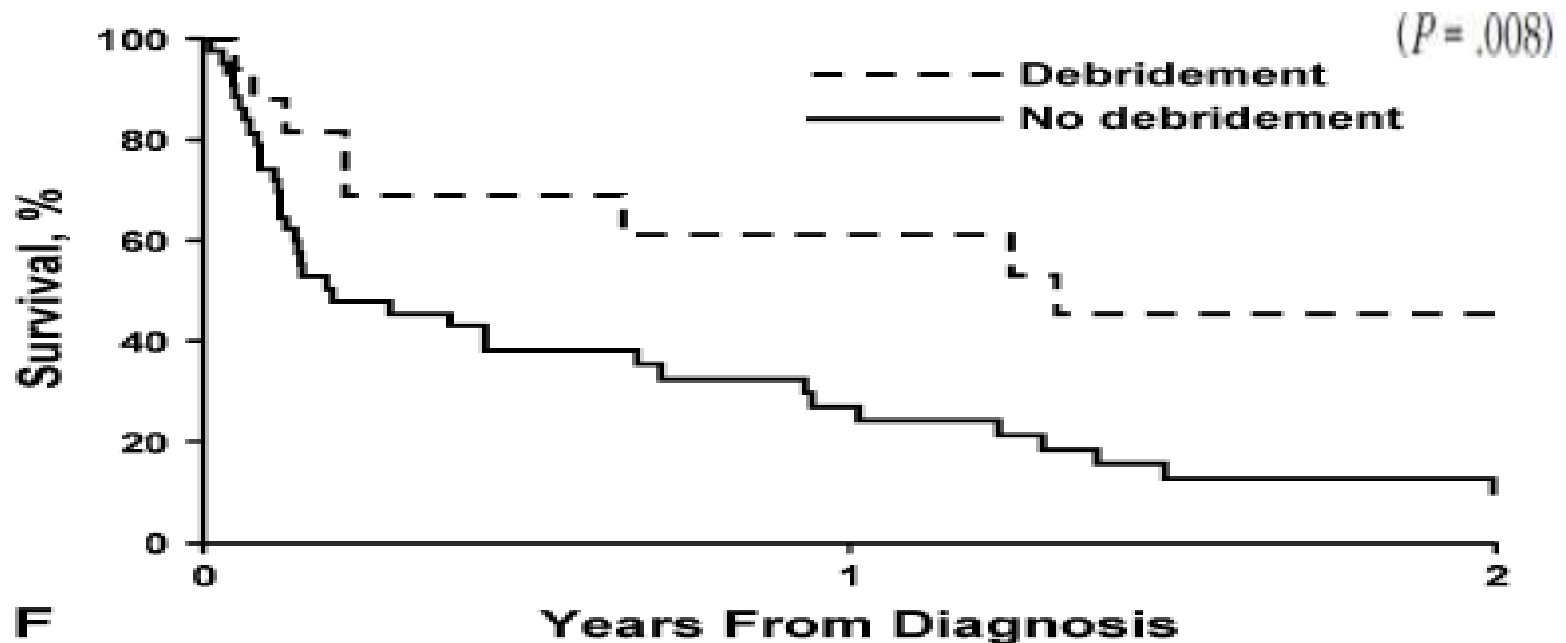
1. wound infection
2. poor wound healing
3. Sepsis
4. Adynamic bone syndrome
5. hypocalcemia
6. hyperphosphatemia.

# **Wound management: the Goal**

1. Control exudate
2. Prevent infection
3. Facilitate wound healing
4. Keep the wound bed free of necrosed devitalized tissue

**Surgical, Chemical, and Maggot debridement**

# Calciophylaxis: Natural history, risk factor analysis, and outcome



The patients were not matched for disease severity or systemic illness

## Should We Perform Surgical Debridement in Calciphylaxis?



We think that the decision to debride in calciphylaxis should be **based on the patient's total condition**, especially because patients with calciphylaxis might have poor wound healing potential because of their comorbidities.

## Clinical report

# Surgical Maggots

Chris Massari<sup>a</sup>, Albert L. Vincent<sup>a</sup>, Veronica T. Tucci<sup>b</sup>, John N. Greene<sup>c</sup>, Chakrapol Sriaroon<sup>a</sup>

<sup>a</sup>*Division of Infectious Diseases and Tropical Medicine, University of South Florida, Tampa, Florida;*

<sup>b</sup>*University of South Florida College of Medicine, Tampa, Florida;* <sup>c</sup>*H. Lee Moffitt Cancer Center & Research Institute, Tampa, Florida, FL 33612-9497, USA*



**Greenbottle fly , *Phaenicia sericata***

# Hyperbaric oxygen

Hyperbaric oxygen therapy was first used in the early 20th century and reappeared in the 1940s as a treatment for deep-sea divers

FDA has approved the therapy for severe heat burns, gangrene and CO poisoning







Controversies and Concerns in Hemodialysis

Series Editor: Marcello Tonelli

## **Calcific Uremic Arteriopathy – The Argument for Hyperbaric Oxygen and Sodium Thiosulfate**

### **ABSTRACT**

Calcific uremic arteriopathy (CUA) is a rare event primarily in patients with end-stage kidney disease which is characterized by small vessel media calcification, panniculitis, dermal necrosis producing exquisitely painful difficult to heal wounds. Mortality rates may be as high as 80%, predominantly due to intervening sepsis. This clinical phenomenon is being increasingly reported and treated with a widening number of agents. Recent case reports highlight the benefit of two modalities that have been employed as adjuvant therapy with significant success in the treatment of CUA. Hyperbaric oxygen (HBO) is

capable of enhancing oxygen delivery to the ulcerating lesions that characterize CUA. Chronic hypoxia can be reversed using HBO to facilitate growth factor production, neoangiogenesis, fibroblast proliferation, and collagen synthesis that may facilitate all aspects of wound healing. Sodium thiosulfate appears to chelate and solubilize calcium ions, reducing the calcium vascular load that appears to participate in the obliterative small vessel disease. There is a rapid analgesic effect and slower regression of cutaneous calcific nodules. The authors advocate for aggressive treatment of CUA, using all available therapies.

## CASE REPORT

### Calcific uremic arteriopathy ameliorated by hyperbaric oxygen therapy in high-altitude area





# Pain Management

- The exact etiology of pain is unclear and is thought to be **ischemic** in origin but there may be a **neuropathic** component associated with nerve inflammation.
- **Opioid** analgesics are typically required to control severe pain, but morphine, codeine, and hydrocodone should be avoided in dialysis patients due to accumulation of neurotoxic metabolite

## *Clinical Note*

# Symptomatic Management of Calciphylaxis: A Case Series and Review of the Literature

Mark N. Polizzotto, MB BS, BMedSc, Tamsin Bryan, MB BS,  
Michael A. Ashby, MB BS, MD, and Peter Martin, MB BCh

*Department of Hematology (M.N.P.), The Alfred Hospital, and Palliative Care Services  
(T.B., M.A.A., P.M.), St. Vincent's Hospital, Melbourne, Victoria, Australia*

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## **Abstract**

*Calciphylaxis, or calcific uremic arteriopathy, is a rare complication of end-stage renal impairment. It is characterized by the development of small vessel vasculopathy with subcutaneous necrosis and ulceration. Intense pain and cutaneous hyperesthesia are prominent features. Mortality rates are high, and the resulting morbidity is significant. While symptomatic management is the mainstay of treatment, it can be challenging. We describe the symptomatic management of a series of three patients with calciphylaxis. Particular emphasis is placed on the use of multimodal analgesia with high-dose opioids, ketamine, and benzodiazepines and on the use of preemptive analgesia.* J Pain Symptom Manage 2006;32:186–190. © 2006 U.S. Cancer Pain Relief Committee. Published by Elsevier Inc. All rights reserved.

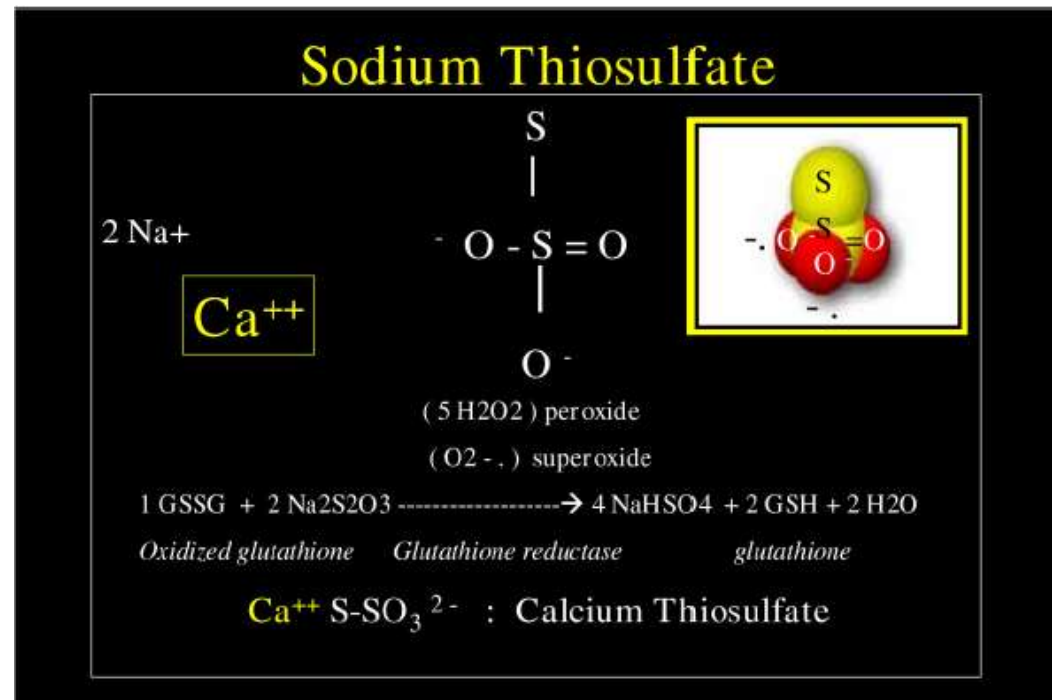
# Na Thiosulphate (STS)



It is a reducing agent  
that forms water-  
soluble complexes  
with many metals and  
minerals

It acts as

1. Antioxidants
2. Vasodilators
3. Ca chelating agent



# Intravenous STS

Sodium thiosulfate was most frequently administered as 25 g intravenously in 100 ml of normal saline given over the last half-hour of each hemodialysis session and this is the currently recommended dose for an average 70 kg person who is on three times a week hemodialysis

Duration of therapy ??

# Sodium Thiosulfate Therapy for Calcific Uremic Arteriopathy

One-year mortality in patients treated with STS was 35%.

## Conclusion

Although conclusive evidence regarding its efficacy is lacking, a majority of patients who received STS demonstrated clinical improvement in this study.





Fellows' Forum in Dialysis

Edited by Mark A. Perazella

### **Unexpectedly Severe Metabolic Acidosis Associated with Sodium Thiosulfate Therapy in a Patient with Calcific Uremic Arteriopathy**

#### **ABSTRACT**

Calcific uremic arteriopathy, formerly known as calciphylaxis is a devastating condition that primarily affects patients with end-stage renal disease. The lesions can progress to massive ulcerations of the subcutaneous tissue that are associated with a high degree of morbidity and mortality, usually related to sepsis. Although the pathophysiology of this condition is poorly understood, it appears to be related to a derangement in calcium-phosphate metabolism. Thus, treatments have focused on the treatment of hyperparathyroidism albeit with

poor results. More recently, sodium thiosulfate (STS) has emerged as a promising therapy following multiple case reports of marked disease regression following its use. As STS is a strong acid, metabolic acidosis has been described following its administration, although relatively mild in degree. We report a case of a patient with calciphylaxis who repeatedly developed a severe anion gap metabolic acidosis following each dose of STS requiring a significant reduction in the dose.

Case Report/Case Series

# Intralesional Sodium Thiosulfate for the Treatment of Calciphylaxis

**IMPORTANCE** Calciphylaxis is a potentially fatal disorder of abnormal calcium deposition. Patients commonly present with painful retiform to stellate purpuric lesions that often undergo ulceration and necrosis, increasing the risk of infection and life-threatening sepsis. Treatment is multifaceted, and improved outcomes have been demonstrated with intravenous sodium thiosulfate; however, the use of this medication can be limited by its adverse effects. The use of topical sodium thiosulfate has been successfully reported for superficial calcium deposits in the skin from other processes. Therefore, we hypothesized that intralesional (IL) sodium thiosulfate may be an effective treatment for the deeper lesions of cutaneous calciphylaxis. We provide a retrospective case review of 4 patients with calciphylaxis who were treated with IL sodium thiosulfate.

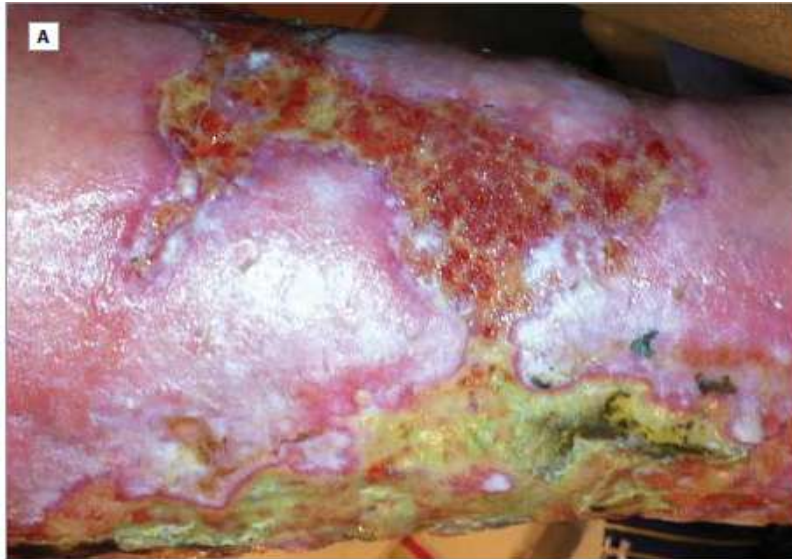
**OBSERVATIONS** Four patients with biopsy-proven cutaneous calciphylaxis were treated with IL sodium thiosulfate (250 mg/mL) in areas of clinically active disease. The patients tolerated the medication well, with only transient localized discomfort during injection. All 4 patients had complete healing of their ulcers and remission of disease.

**CONCLUSIONS AND RELEVANCE** Intralesional sodium thiosulfate may be an effective and well-tolerated treatment for localized calciphylaxis. This novel approach requires further research and investigation.



# Intra-lesional sodium thiosulfate in calciphylaxis





A, Large ulceration on the posterior aspect of the leg extends circumferentially, with surrounding purpura indicating active disease. B, As the ulcer gradually decreased in size, remaining areas of purpura were injected with sodium

thiosulfate. C, At 12 weeks, the ulcer was nearly healed, with no signs of active disease. D, Six months after presentation, the ulcerations had healed.

# Dialysis modality and dialysis prescription

- Dialysis prescription should be optimized to achieve the recommended goals of dialysis adequacy.
- In the literature, peritoneal dialysis is described to confer higher calciphylaxis risk when compared to hemodialysis , however, some experiences are not consistent with this observation

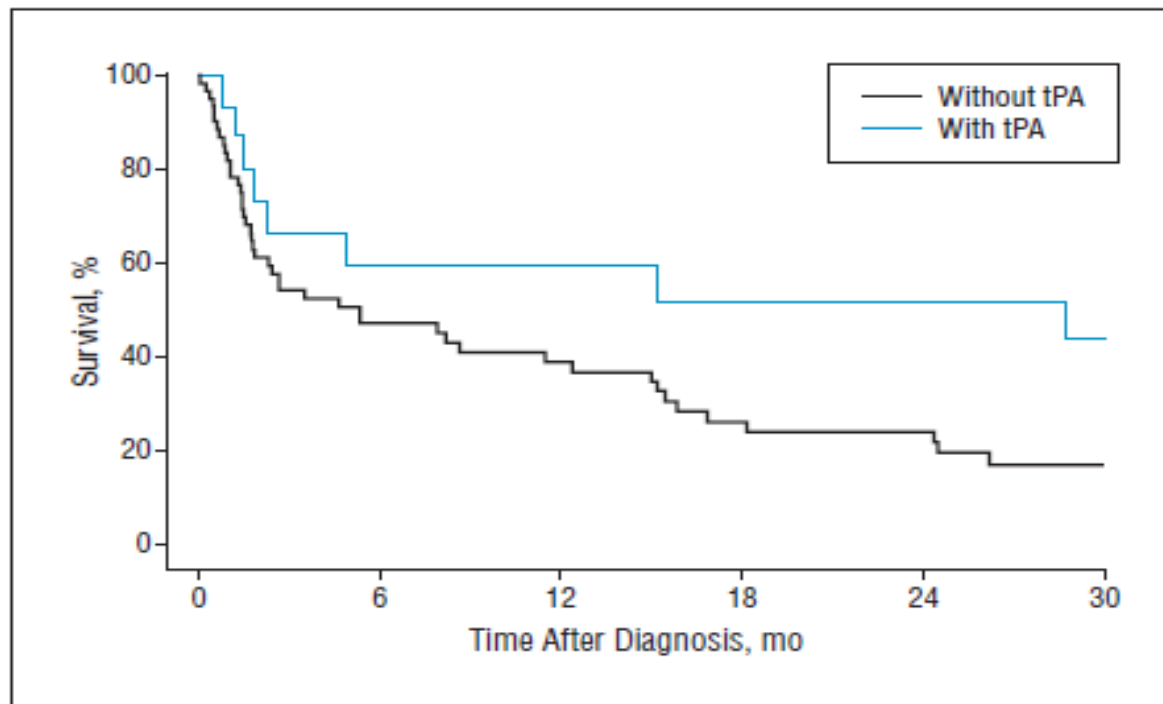


# Nutrition Support



# Retrospective Analysis of Tissue Plasminogen Activator as an Adjuvant Treatment for Calciphylaxis

Rokea A. el-Azhary, MD, PhD; Allison K. Arthur, MD; Mark D. P. Davis, MD; Marian T. McEvoy, MD; Lawrence E. Gibson, MD; Amy L. Weaver, MS; Michael J. Camilleri, MD; David A. Wetter, MD; Roger H. Weenig, MD





## Multi-intervention Management of Calciphylaxis: A Report of 7 Cases

*Corisande Baldwin, MD,<sup>1</sup> Myriam Farah, MD, FRCPC,<sup>2</sup> Marianna Leung, PharmD,<sup>2</sup>  
Paul Taylor, MB, FRCPC,<sup>2</sup> Ronald Werb, MB, FRCPC,<sup>2</sup> Mercedeh Kiaii, MD, FRCPC,<sup>2</sup>  
and Adeera Levin, MD, FRCPC<sup>2</sup>*

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Calcific uremic arteriolopathy (calciphylaxis) is a devastating but rare complication seen predominantly in dialysis patients that often is fatal. Because of the rarity of the disease and the multifactorial nature of its cause, no clinical trials have been conducted to date to determine the best therapy for the condition. We report a case series of 7 patients at a single institution in whom a systematic multi-interventional treatment strategy was implemented, consisting of trigger-agent cessation (calcium-based phosphate binders, alphacalcidol, and warfarin), wound management, and antibiotic therapy, supplemented by intensified hemodialysis (4 hours daily for 7 days followed by 5-6 times weekly), intravenous sodium thiosulfate (12.5-25 g intravenously 3 times a week), and attempted oxygen therapy (given through a face mask or hyperbaric chamber as tolerated by patient circumstance). Treatments selected were based on literature review, consensus discussion, and attempts to address the physiologic disturbances that underlie the condition. All 7 patients identified with biopsy-proven calcific uremic arteriolopathy were treated with this regimen in 2007-2010, with 6 of 7 showing complete recovery. We suggest that consistent implementation of a multi-interventional approach may alter the course of this devastating disease. Further studies are needed to confirm and extend these findings.

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## ORIGINAL ARTICLE

# Multimodal treatment of calcific uraemic arteriolopathy (calciophylaxis): a case series

## Abstract

**Background:** This is an incident series of five dialysis patients with late-diagnosed calcific uraemic arteriolopathy (CUA), severe uncontrolled hyperparathyroidism and infected skin ulcerations.

**Methods:** A multimodal intervention was based on wound care, antibiotics, surgical debridement, sodium thiosulphate and cinacalcet and associated with regression of skin disease in four cases after varying treatment time periods ranging from 4 to 33 months.

**Results:** Multimodal treatment including sodium thiosulphate and cinacalcet was associated with very favourable local outcomes and survival. This series further confirms that the diagnosis of CUA is rarely made at the nodular, non-ulcerative phase of the disease.

**Conclusions:** This series contributes to the build-up of case series reporting on the treatment of CUA, and will hopefully serve as a basis of well-conceived comparative effectiveness studies investigating the value of the combined interventions applied so far in this severe condition.

**Key words:** calcific uraemic arteriolopathy, cinacalcet, CUA, parathyroid hormone, skin ulcers



## Calciophylaxis from Nonuremic Causes: A Systematic Review

Table 1. Causes of nonuremic calciophylaxis<sup>a</sup>

Conclusion: Calciophylaxis should be considered while evaluating skin lesions in patients with predisposing conditions even in the absence of end-stage kidney disease and renal transplantation. Nonuremic calciophylaxis is reported most often in white women. Mineral abnormalities that are invoked as potential causes in calcific uremic arteriolopathy are often absent, suggesting that heterogeneous mechanisms may contribute to its pathogenesis. Nonuremic calciophylaxis is associated with high mortality, and there is no known effective treatment.

C and S deficiency	
Crohn disease	1 (2.8)
Osteomalacia treated with nadroparin calcium	1 (2.8)
POEMS syndrome	1 (2.8)
Vitamin D deficiency	1 (2.8)
Weight loss	1 (2.8)
CKD (not ESKD)	1 (2.8)

# Conclusion

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you*

